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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/917,378	07/28/2001	Shi-You Ding	NREL 01-35	9985

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PAUL J WHITE, SENIOR COUNSEL
NATIONAL RENEWABLE ENERGY LABORATORY (NREL)
1617 COLE BOULEVARD
GOLDEN, CO 80401-3393

EXAMINER	
RAO, MANJUNATH N	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 08/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/917,378	DING ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- Th MAILING DATE of this communication appears on the c ver sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 May 2003 and 09 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,26-34,43,44 and 63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *10,11,26-34,43,44 and 63* is/are allowed.

6)☒ Claim(s) *1-9 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-12, 26-34, 43-44, 63 are still at issue and are present for examination.

Applicants' amendments and arguments filed on 5-1-03, paper No.17 and 6-9-03, paper No.19, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

Claim 26 is objected to because of the following informalities: Claim 26 has sub parts claimed as a), b) or d). The claim is either missing sub part c) or has been mislabeled as sub part d). Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 and claims 2-9 which depend therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites the phrase "catalytic domain glycoside hydrolase family (GH5)". It is not clear to the Examiner as to what applicants mean by the above phrase. It appears that applicants meant to "catalytic domain of glycoside hydrolase family (GH5)". If this is so amending the claim accordingly would overcome this rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a mannanase polypeptide comprising a catalytic domain classified in GH5 family, with SEQ ID NO:3, and further comprising a CBD-III domain with SEQ ID NO:4 and a CBD-II domain with SEQ ID NO:5, or a polypeptide having SEQ ID NO:1 encoded by a nucleic acid sequence with SEQ ID NO:2, does not reasonably provide enablement for any or all such polypeptides comprising catalytic domain of any glycoside hydrolase of family 5 and further comprising a CBD III, a CBD II and a signal peptide or any industrial detergent mixture comprising such mannanase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-5, 12 are so broad as to encompass any polypeptide comprising catalytic domain of any glycosylhydrolase belonging to family 5. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large

number of polypeptides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only one such mannanase whose catalytic domain is classified in family 5. It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides having catalytic domain of all or any glycosylhydrolase belonging to family 5 in order to degrade hemi cellulose, some even with an undefined function/activity. The specification is limited to teaching use of SEQ ID NO: 1 or a polypeptide comprising contiguous polypeptides with SEQ ID NO:3,4, 5 as a mannanase polypeptide but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any glycosylhydrolase polypeptide in family 5 as described in the above paragraphs because the specification does not establish: (A) regions of the protein structure which may be modified without effecting either the catalytic activity or the cellulose binding activity of the CBD domains; (B) the general tolerance of glycosylhydrolases such as to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any glycosylhydrolase or any CBD polypeptide amino acid residues with an expectation of obtaining the desired biological function i.e., to function as mannanase; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including all or any glycosylhydrolase catalytic domain belonging to family 5, and cellulose binding domains with an enormous number of amino acid modifications. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re

Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polypeptides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office action applicants have traversed the above rejection as applied to original claims 1-5 and 12-13. Applicants argue that the GH5, CBDII and CBDIII are all well documented in the art and those skilled in the art understand and appreciate that there are a variety of sequences characterized in these families and furthermore techniques are well known in order to assemble these sequences. However, in view of the claim amendments, Examiner has withdrawn the previous rejection and re-written the above rejection as it applies to the amended claim 1. In view of the claim amendments to claim 26, Examiner has also withdrawn the rejection of claims 26-33 under 35 U.S.C. 112, Ist paragraph as being non-enabled. Examiner suggests applicants to amend claim 1 to recite "...the mannanase peptide comprising a mannanase catalytic domain classified in glycoside hydrolase family 5, a carbohydrate binding domain ...", which would overcome the above rejection.

Claims 1-5, 12, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-5, 12 are directed to composition comprising a mannanase peptide wherein said mannanase peptide comprises a catalytic domain GH5 of 370-380 amino acids in length, a

carbohydrate binding domain CBD type III of 140-160 amino acids in length and a CBD type II of 95-110 amino acids in length and a signal peptide of unknown amino acid length. Claims 1-5, 12 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides including modified polypeptide sequences, modified by at least one of deletion, addition, insertion and substitution of an amino acid residue that have not been disclosed in the specification. No description has been provided of even a representative number of polypeptide sequences encompassed by the claim. No information, beyond the characterization of SEQ ID NO:1 or characterization of SEQID NO:3-5 as catalytic domains and CBD domains, has been provided by applicants which would indicate that they had possession of the claimed genus of all the polypeptides. The specification does not contain any disclosure of the structure of the polypeptide sequences, including fragments and variants within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of structures. Therefore many structurally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous Office action, applicants have responded to the rejection of claims as not enabled. However, their response is silent to the rejection under written description requirement.

Examiner has withdrawn the rejection of previous claims 28-35, 44-45 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, in view of amendments to claims 26 and the above claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Gibbs et al. (Appl. Environ. Micorbiol., 1992, Vol. 58(12):3864-3867). This rejection is based upon the public availability of a printed publication more than one year prior to the filing date of the instant application. Claims 1-4 of the instant application are drawn to a composition comprising a substantially purified mannanase A peptide, wherein the mannanase peptide comprises a catalytic domain, a carbohydrate binding domain (CBD) III and a CBD II, wherein the mannanase further comprises a linker and a signal peptide and wherein the catalytic domain

comprises an amino acid sequence that is about 370 to about 380 residues long and wherein the CBDs III is defined by a sequence of 140-160 amino acids respectively. Gibbs et al. disclose an identical composition comprising a mannanase catalytic domain linked to two CBDs (see the entire publication especially figure 2, panel C). Even though the reference does not disclose as to whether the CBDs are CBD III and CBD II. Examiner takes the position that the CBDs in the reference and the CBDs claimed are one and the same. Thus Gibbs et al. anticipate claims 1-5 of this application as written.

Since the Office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

In response to the previous Office action applicants have refuted the above rejection based on the arguments used against the enablement rejection and have also filed a Rule 1.32 declaration of Dr. Ding declaring that both CBDs in the Gibbs et al. reference belong to the CBD II category as opposed to the instant invention comprising CBD II and CBDIII. The declaration does not provide any scientific basis for the identification of the two CBDs in the reference. Applicants also erroneously argue that amended claim 1 specifically refers to SEQ ID NO:3. A perusal of amended claim 1 indicates that claim 1 continues to be independent of any SEQ ID NO. Based on these arguments, applicants conclude that the reference does not anticipate above claims. The Declaration by Dr.Ding does not state scientific reasons why she believes that the two CBDs are CBDII and not CBD II and CBDIII as alleged by the Examiner.

There is no evidence presented within the declaration in support of the conclusion. As such Examiner considers that the declaration merely presents an opinion by one of skill in the art. While such opinion is entitled to consideration the probative value must be assessed in view of the strength of any opposing evidences and the interest of the Declarant in the outcome of the case and the amount of factual evidence to support the evidence to support the opinion (see MPEP 716.01.c.). Therefore in view of the absence of scientific evidence against Examiner's assertion that the reference discloses a mannanase comprising CBD II and CBDIII domains, Examiner continues to maintain the above rejection as it applies to claims 1-4. Examiner has withdrawn the above rejection of claim 5 based solely on applicant's argument that the second CBD in the reference comprises 155 amino acids as opposed to that claimed in the claim 5.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gibbs et al. as applied to claims 1-4 above, and further in view of Liu et al. (US 6,126,698 10-3-2000). Claims 12 is drawn to industrial detergent mixtures suitable for degrading hemi cellulose comprising the mannanase in the detergent. The reference of Gibbs et al. as it applies to the mannanases has been described above.

Liu et al. described the use of mannanase for degradation of hemi cellulose and a mixture of enzymes that can be used along with a detergent in textile industry for biopolishing of fabrics.

Liu et al. also teach that CBDs confer high binding to cellulose targets and lead the enzyme to the interior depths of a cellulose fiber. With the reference of Gibbs et al. in hand disclosing a new multidomain mannanase comprising two CBDs, it would have been obvious to one of ordinary skill in the art to use such a mannanase in a industrial mixture as taught by Liu et al. One of ordinary skill in the art would be motivated to do so as the newly disclosed mannanase has two CBDs and would be an ideal candidate for such uses. One of ordinary skill in the art would have a reasonable expectation of success since Gibbs et al. provide the enzyme and Liu et al. readily provide a use for such an enzyme.

Therefore, the above invention would have been *prima facie* obvious to one of ordinary skill in the art.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

In response to the above rejection applicants argue that even if Gibbs and Liu et al. are indiscriminately combined they still fail to teach of suggest the composition of amended claim 1. Applicant also argues that there is no suggestion to modify either reference in a manner that describes the mannanase composition of amended claim 1. Examiner respectfully disagrees. It is also not clear to the Examiner as to how amended claim 1 overcomes the above rejection.

Examiner has already discussed the rejection of claim 1 above. Contrary to applicants argument, Examiner asserts that Gibbs et al. and Liu et al. render claim 12 *prima facie* obvious to one of ordinary skill in the art.

Conclusion

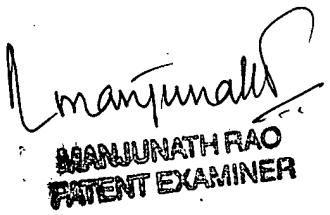
Claims 10, 11, 26-34, 43-44 and 63 are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura

Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.



Manjunath N. Rao
August 20, 2003